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Low-Level Lead Exposure, Intelligence and Academic Achievement: A Long-term Follow-up Study

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ABSTRACT. The implications of low-level lead exposure for children's intellectual and academic performance at school age are uncertain. This issue was investigated in a prospective study of middle-class and upper-middle-class children with low lifetime exposures to lead. A battery of neuropsychological tests was administered at age 10 years to 148 children whose lead exposure and cognitive function had been previously assessed at ages 6, 12, 18, 24, and 57 months. Primary endpoints were Wechsler Intelligence Scale for Children-Revised (WISC-R) and the Kaufman Test of Educational Achievement (K-TEA). Higher levels of blood lead at age 24 months, but not at other ages, were significantly associated with lower global scores on both the WISC-R and the K-TEA after adjustment for potential confounders. Over the range of approximately 0 to 25 $\mu\text{g}/\text{dL}$, a 0.48- $\mu\text{mol}/\text{L}$ (10 $\mu\text{g}/\text{dL}$) increase in blood lead at 24 months was associated with a 5.8-point decline in WISC-R Full-Scale IQ (95% confidence interval: 1.7 to 9.9, $P = .007$) and an 8.9-point decline in K-TEA Battery Composite score (95% confidence interval: 4.2 to 13.6, $P = .0003$). Mean blood lead level at age 24 months was 0.31 $\mu\text{mol}/\text{L}$ (6.5 $\mu\text{g}/\text{dL}$; SD: 4.9, 90th percentile: 12.5). Slightly elevated blood lead levels around the age of 24 months are associated with intellectual and academic performance deficits at age 10 years. *Pediatrics* 1992;90:855-861; lead, intelligence, achievement, neuropsychological toxicology, environmental epidemiology.

ABBREVIATIONS. WISC-R, Wechsler Intelligence Scale for Children-Revised; K-TEA, Kaufman Test of Educational Achievement-Brief Form; HOME, Home Observation for Measurement of the Environment; GCI, General Cognitive Index; pb24, 24-month blood lead level; CI, confidence interval.

Lead poisoning is considered the most important pediatric environmental health problem in the United States.¹ Blood lead levels in the range of 0.48 to 0.97 $\mu\text{mol}/\text{L}$ (10 to 20 $\mu\text{g}/\text{dL}$) have been linked to a variety of adverse health effects² and serve as reference points for recent revisions in the screening and treatment protocols recommended by the Centers for Disease Control.¹ The long-term implications of expo-

sure producing blood lead levels in this range remain uncertain, however. In primates, early exposures producing peak blood lead levels of 1.21 $\mu\text{mol}/\text{L}$ (25 $\mu\text{g}/\text{dL}$) and steady-state levels of 0.63 $\mu\text{mol}/\text{L}$ (13 $\mu\text{g}/\text{dL}$) impair performance up to 10 years later on a variety of cognitive tasks.³ Some ongoing prospective studies,^{4,5} but not all,^{6,7} report cognitive deficits at preschool age among children with similar early exposures. The results of another study are mixed.⁸ No prospective study has yet reported to what extent any early deficits persist to school age. We report here on the association between early lead exposure and children's intellectual functioning and academic achievement at age 10 years.

METHODS

Sample

Infants born at the Brigham and Women's Hospital (Boston, MA) between August 1979 and April 1981 were provisionally eligible if the umbilical cord blood lead level was below the 10th percentile ($<0.15 \mu\text{mol}/\text{L}$ or 3 $\mu\text{g}/\text{dL}$), approximately at the 50th percentile (0.31 $\mu\text{mol}/\text{L}$ or 6.5 $\mu\text{g}/\text{dL}$), or greater than the 90th percentile ($\geq 0.48 \mu\text{mol}/\text{L}$ or 10 $\mu\text{g}/\text{dL}$) ("low," "medium," and "high" prenatal exposure, respectively). Other eligibility criteria included (1) absence of medical conditions associated with developmental handicap, (2) English as the first language, (3) residence in the Boston area ($<19 \text{ km}$ from The Children's Hospital but not in certain public housing projects), and (4) maternal consent to be contacted.⁹ A total of 249 infants were enrolled. Postnatal blood lead levels and development were assessed at ages 6, 12, 18, 24, and 57 months. The base population for the 10-year follow-up assessment was the 169 children from the original sample who were tested at age 57 months.⁵ Assessments were completed on 148 children (87.6% of those considered eligible; 59.4% of the original cohort). Nine families refused or repeatedly failed to keep appointments (5.3%), 4 had moved from the area (2.4%), and 8 could not be located (4.7%). The cohort generally consisted of white, intact families with college-educated parents and relatively high-functioning children with low lifetime exposures to lead (Table 1). Compared with eligible families that did not participate in the 10-year assessment, participants tended to be of relatively higher socioeconomic status and to provide slightly more optimal developmental environments for their children.

Neuropsychological Assessment

The children were administered a battery of tests by a psychologist (K.M.S.) who was "blind" to all aspects of a child's developmental and lead exposure histories. In most cases, testing was conducted at The Children's Hospital (Boston) in a single session lasting approximately 3 hours. A second session was required to complete the testing of two children, and seven children were tested in their homes. The mean age (SD, range) of the children at testing was 9 years 9 months (41 days, 9 years 7 months to 10 years 2 months).

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Children's Full-Scale IQ scores on the Wechsler Intelligence Scale for Children-Revised (WISC-R)⁴ and Battery Composite scores on the Kaufman Test of Educational Achievement-Brief Form (K-TEA)⁵ are considered the primary endpoints. The other tests in the battery are considered secondary endpoints, which may shed light on the bases for any exposure-related performance differences on the WISC-R or K-TEA. Analyses of these secondary endpoints will be presented in a separate report.

Measurement of Potential Confounders

Parents completed several questionnaires: medical and educational history of the child, family structure and sociodemographic characteristics, Family Adaptability and Cohesion Evaluation Scales,¹⁰ Social Readjustment Rating Scale,¹¹ Parenting Stress Index,¹² Children's Life Events Inventory-Revised (modified),¹³ and Social Support Network.¹⁴ Based on a brief interview with the parent, the psychologist completed Scales V (Provision for Active Stimulation) and VI (Family Participation in Developmentally Stimulating Experiences) of the Home Observation for Measurement of the Environment (HOME) Inventory (Elementary).¹⁵ Information about many other potential confounders was available in records from previous assessments (eg, maternal IQ, birth weight, HOME scores).

Blood Sampling and Analysis

A Children's Hospital phlebotomist drew 5-mL venous blood samples from 116 children on the day of testing. Samples were not obtained from 32 children because of refusal or because the assessment was conducted at home. A portion of each sample was sent to the Clinical Laboratories of the Children's Hospital for serum ferritin measurement by an immunoenzymatic assay using monoclonal antibodies. The remainder of the sample was sent to ESA Laboratories (Bedford, MA), where blood lead concentration was measured in duplicate using graphite furnace atomic absorption spectrophotometry with Zeeman Background correction using a Hitachi model Z-9000.²⁰ Quality control samples (low and high bench samples and low and high blind samples provided by the Centers for Disease Control) were included among sample batches to monitor performance of the analytical system.

Mean blood lead level was 0.14 $\mu\text{mol/L}$ (2.9 $\mu\text{g/dL}$, SD: 2.4, range: 0.5 to 16). Seven additional measures of the children's lead exposure were available: blood lead levels at birth (cord blood), 6, 12, 18, 24, and 57 months, and for 78 children, tooth lead level. Due to the limited data available, no analyses involving tooth lead level are reported. The median correlation among the various blood lead levels was 0.24 (range 0.66 to 0.02).

TABLE 1. Characteristics of Families Participating in 10-Year Assessment

Family social class,* % class 1	58.1
Maternal education, % college graduate	64.9
Paternal education, % college graduate	66.2
Maternal IQ†	125.0 (15.7)¶
HOME‡ total (57 mo)	51.4 (3.7)¶
Sex, % male	50.7
Race, % white	94.6
Birth order, % firstborn	56.1
Life events§	123.2 (107.7)¶
General Cognitive Index (57 mo)	116.0 (14.9)¶
Blood lead history, $\mu\text{g/dL}$	
57 mo	6.3 (3.8)¶
24 mo	6.5 (4.9)¶
18 mo	7.8 (5.7)¶
12 mo	7.7 (6.5)¶
6 mo	6.7 (7.0)¶
Cord blood, % $\geq 10 \mu\text{g/dL}$	28.6

* Hollingshead Four-Factor Index of Social Class.

† Peabody Picture Vocabulary Test.¹⁰

‡ Home Observation for Measurement of the Environment.¹⁵

§ Social Readjustment Rating Scale.¹¹

|| McCarthy Scales of Children's Abilities.⁵

¶ Mean (SD).

Statistical Methods

The association between children's lead exposure and their neuropsychological performance was evaluated by multiple regression, adjusting for potential confounders. Because the correlates of a child's blood lead level may change over time, a separate confounder selection process was carried out for each age at which blood lead level was measured. As the endpoint of highest priority, WISC-R Full-Scale IQ score was used to identify correlates of test performance.

The process by which covariates were selected for inclusion in the regression models was based on a combination of empirical and subject matter considerations. The primary goal was to include the variables necessary to obtain an unbiased estimate of the association between lead exposure and performance. Following the recommendation of Dales and Lry²¹ and Mickey and Greenland,²² we considered variables associated with both Full-Scale IQ and a particular blood lead measurement at a *P* value of .25 or less to be potential confounders. The secondary goal was to increase the precision of the estimate. To this end, we also included factors generally acknowledged to be important antecedents or correlates of cognitive development but which did not necessarily meet the empirical criteria for a confounder²³ (eg, maternal IQ, birth order, sex). The result was a unique set of 8 to 13 variables for each of the seven blood lead measurements. For a given blood lead measurement, the model derived for Full-Scale IQ was employed in the analyses of other endpoints.

To assess the impact of confounder selection strategy, additional regression analyses were conducted, including as confounders factors selected using a change-in-estimate criterion,²⁴ ie, variables whose addition to the bivariate regression of Full-Scale IQ on lead produced more than a 10% change in the lead coefficient.

Coefficients associated with postnatal blood lead levels represent the estimated change in outcome score (eg, IQ) for each increase of 0.05 $\mu\text{mol/L}$ (1 $\mu\text{g/dL}$) in blood lead level. Umbilical cord blood lead level was fitted as two indicator variables representing membership in the "low" and "medium" exposure groups. Coefficients represent the estimated differences between the scores of children in these groups and children in the "high" exposure group.

The sensitivity of the models was evaluated in several ways. Standard regression diagnostics were used to identify influential observations,²⁵ and models were refitted, deleting observations with large residuals or with large impact on either the regression coefficients or fitted values. Various model reduction strategies were explored, including stepwise backward elimination and all subsets (optimal) regression. Model specification was evaluated by examining the impact of including additional variables: terms representing a child's average blood lead level across various age intervals; maximum blood lead level in the first year, the second year, or over the course of the study; interaction terms combining blood lead level and each of the other predictors; measures of marital and maternal psychiatric factors; serum ferritin level; and General Cognitive Index (GCI) score achieved at age 57 months on the McCarthy Scales of Children's Abilities.⁵

All analysis were carried out using PC-SAS.²⁶ All *P* values are two-tailed.

RESULTS

Overall Performance

Children's WISC-R and K-TEA scores were approximately 1 SD above the population average. Mean (SD, range) Full-Scale, Verbal, and Performance IQ scores were 119.1 (14.8, 71 to 147), 118.1 (14.9, 67 to 146), and 115.9 (14.2, 78 to 146), respectively. Mean (SD, range) Battery Composite, Mathematics Composite, Reading Composite, and Spelling scores were 118.8 (16.3, 69 to 160), 122.1 (18.7, 70 to 160), 117.0 (14.0, 71 to 140), and 113.5 (17.1, 68 to 153), respectively.

Wechsler Intelligence Scale for Children-Revised

Crude Analyses. All postnatal blood lead levels were inversely associated with Full-Scale IQ measured at 10 years of age, although only the associations in-

volving blood lead levels at age 10 years, 57 months, and 24 months were statistically significant (Table 2). This was also true for both Verbal and Performance IQ scores.

Adjusted Analyses. Adjustment for confounding reduced the magnitude of the coefficients associated with all blood lead levels. The coefficient associated with 24-month blood lead level (pb24) remained significant (Table 2). The decline in children's Full-Scale IQ corresponds to 5.8 points per 0.48 $\mu\text{mol/L}$ (10 $\mu\text{g/dL}$) increase in pb24 (95% confidence interval [CI]: 1.7 to 9.9 points). Adding pb24 to the covariate model accounted for an additional 3.2% of the variance in Full-Scale IQ scores. The partial regression residual plot indicated that this association was linear across the range of pb24 levels in this cohort. Adjusted mean Full-Scale IQ scores are shown for children in pb24 categories corresponding to 0.24- $\mu\text{mol/L}$ (5- $\mu\text{g/dL}$) increments (Figure).

Coefficients associated with a child's average blood lead level between 24 and 57 months or between 24

months and 10 years were greater (although less precise) than the coefficient associated with pb24 alone (-0.82 , $\text{SE} = 0.28$, $P = .004$ and -0.86 , $\text{SE} = 0.34$, $P = .013$, respectively, vs -0.58 , $\text{SE} = 0.21$, $P = .007$). The timing of exposure appeared to be more important than magnitude alone. No index of a child's maximum blood lead level during various age intervals (first year, second year, or lifetime) was significantly associated with Full-Scale IQ (coefficients of -0.13 , -0.35 , -0.20 , respectively).

At the 57-month assessment, higher levels of pb24 were associated with lower GCI scores.⁵ To evaluate whether the association between pb24 and 10-year Full-Scale IQ was due simply to the high correlation between GCI and IQ in this cohort ($r = .71$), IQ was adjusted for GCI in addition to the other 11 variables. The pb24 coefficient in this model was -0.42 ($\text{SE} = .17$, $P = .018$).

The sensitivity analyses indicated that the association between pb24 and Full-Scale IQ was robust to different specifications of the model, to different

TABLE 2. Regression Coefficients Associated With Blood Lead Levels and Children's Wechsler Intelligence Scale for Children-Revised IQ Scores at 10 Years of Age.

Blood Lead Measurement*	Crude: Full-Scale IQ	Adjusted†		
		Full-Scale IQ	Verbal IQ	Performance IQ
10 y	-1.53 (0.56)‡ .008§	-0.46 (0.52) .38	-0.59 (0.53) .27	-0.17 (0.55) .76
57 mo	-0.90 (0.33) .008	-0.26 (0.29) .37	-0.07 (0.30) .80	-0.44 (0.31) .16
24 mo	-0.71 (0.25) .005	-0.58 (0.21) .007	-0.63 (0.22) .004	-0.39 (0.23) .091
18 mo	-0.28 (0.21) .20	-0.12 (0.18) .53	-0.20 (0.19) .30	-0.00 (0.20) .99
12 mo	-0.20 (0.19) .28	-0.00 (0.16) .99	-0.13 (0.16) .42	0.14 (0.17) .39
6 mo	-0.20 (0.18) .29	-0.13 (0.15) .39	-0.24 (0.16) .14	0.03 (0.16) .83
Cord				
Low	-1.29 (3.03) .86#	-0.48 (2.65) .57	-0.98 (2.69) .43	0.23 (2.83) .85
Med¶	-1.52 (3.01)	-2.55 (2.56)	-3.31 (2.61)	-1.21 (2.74)

* Age at which blood lead level was measured.

† Variables included in models:

10 years: HOME120 (sum of Scales V and VI of the Home Observation for Measurement of the Environment at age 10 years), family stress, child stress, maternal age, race (white/nonwhite), birth weight, maternal IQ, number of day-care situations through 57 months, HOME57 (total score at 57 months), socioeconomic status (SES), sex, birth order (first, second, third or later), marital status (married/not married)

57 months: HOME120, family stress, child stress, race, maternal IQ, HOME57, SES, sex, birth order, marital status

24 months: HOME120, child stress, maternal age, race, maternal IQ, HOME57, SES, sex, birth order, marital status, number of residence changes prior to age 57 months

18 months: HOME120, family stress, child stress, maternal age, race, maternal IQ, HOME57, SES, sex, birth order, marital status, number of residence changes prior to age 57 months

12 months: HOME120, child stress, race, maternal IQ, HOME57, SES, sex, birth order, marital status, family balance (Family Adaptability and Cohesion Evaluation Scales-III), parent's sense of competence

6 months: HOME120, child stress, race, maternal IQ, HOME57, SES, sex, birth order, marital status
Cord blood: child stress, maternal age, maternal IQ, HOME57, SES, sex, birth order, number of residence changes prior to age 57 months, race.

‡ Regression coefficient (SE), representing the estimated change in score associated with each 0.48- $\mu\text{mol/L}$ (1- $\mu\text{g/dL}$) increase in blood lead level.

§ Two-sided P value associated with the hypothesis that the coefficient is zero.

|| Coefficient (SE) associated with membership in the "low" cord blood lead group ($<3 \mu\text{g/dL}$); reference group is children in the "high" cord blood lead group.

¶ Coefficient (SE) associated with membership in the "medium" cord blood lead group (6 to 7 $\mu\text{g/dL}$); reference group is children in the "high" cord blood lead group.

Two-sided P value associated with the hypothesis that there are no differences among the scores of children in the three cord blood lead groups.

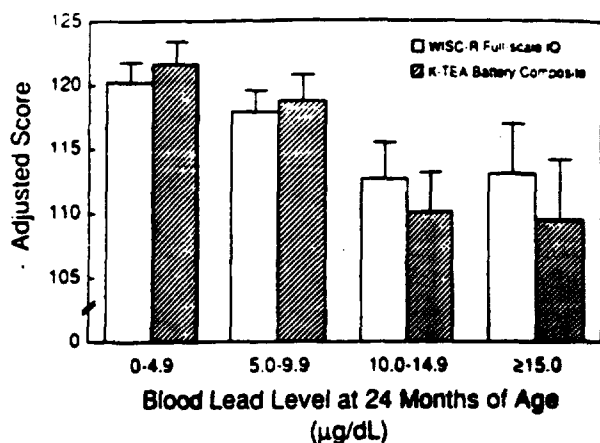


Figure. Mean (\pm SE) adjusted Wechsler Intelligence Scale for Children-Revised (WISC-R) Full-Scale IQ scores and Kaufman Test of Educational Achievement-Brief Form (K-TEA) Battery Composite scores for children classified by blood lead concentration at age 24 months (pb24). Scores are adjusted for Home Observation for Measurement of the Environment (HOME) score at 10 years (Scales V and VI), total HOME score at 57 months, child stress, maternal age, race, maternal IQ, socioeconomic status, sex, birth order, maternal marital status, and number of family residence changes prior to age 57 months. The number of observations by pb24 stratum are 58 (57 for K-TEA score), 47, 18, and 10 for 0 to 4.9, 5.0 to 9.9, 10.0 to 14.9, and ≥ 15 $\mu\text{g}/\text{dL}$, respectively.

model reduction or confounder selection strategies, and to the deletion of influential observations. In most analyses, the change in the pb24 coefficient was less than 15%. The largest change was a 40% reduction (-0.58 to -0.34) when observations with large impact on fitted values were deleted.

Pb24 was also significantly associated at $P < .05$ with Verbal IQ and five WISC-R subtest scores (Arithmetic, Comprehension, Similarities, Picture Completion, Block Design) and at $P < .10$ with two others (Vocabulary, Digit Span). It was not significantly associated with Performance IQ. Children with pb24 levels greater than 10 $\mu\text{g}/\text{dL}$ were less likely than children with lower levels to have Verbal IQs that were significantly higher (≥ 12 points) than their Performance IQs.²⁶ No distinct pattern of relative strengths and weaknesses was apparent in subtest scores, however, nor was the amount of scatter in subtest scores (defined as the number of subtest scores deviating from the overall mean subtest score by at least 1 SD)²⁶ associated with pb24.

Kaufman Test of Educational Achievement

Crude Analyses. Blood lead levels measured at ages 10 years, 24, 18, and 12 months were significantly related to children's Battery Composite scores (Table 3). Each of these blood lead levels was also significantly associated with one or more of the subtest scores (data not shown).

Adjusted Analyses. Only blood lead levels at 24 months of age were significantly associated with adjusted K-TEA scores. Battery Composite score declined 8.9 points for each 0.48- $\mu\text{mol}/\text{L}$ (10- $\mu\text{g}/\text{dL}$) increase in pb24 (95% CI: 4.2 to 13.6) (Table 3) (Figure). Including Full-Scale IQ in the model reduced but did not eliminate the association (coefficient =

-51 ; SE = 0.20, $P = .013$). Exposure-related decreases were also noted in Spelling scores (95% CI: 4.2 to 15.3 points per 0.48- $\mu\text{mol}/\text{L}$ increase) and Mathematics Composite scores (95% CI: 3.4 to 14.8 points per 0.48- $\mu\text{mol}/\text{L}$ increase). Pb24 was more strongly associated with performance on the more advanced Concepts/Applications items (coefficient = -24 , SE = .08, $P = .004$) than on the Computation items (coefficient = -08 , SE = .05, $P = .099$).

DISCUSSION

The most striking finding in this long-term follow-up study is the continued presence at age 10 years of an association noted at age 5 years between a child's blood lead level at 24 months of age and cognitive function. Terms integrating blood lead level over various intervals beginning at 24 months of age were also associated with children's performance. These associations were evident in broad-based assessments of both intelligence and academic achievement. Because the association between pb24 and IQ was apparent even with adjustment for GCI scores achieved at 57 months, the underlying process may involve more than simple persistence of the performance deficits noted at that time. One possibility is that lead exposure around the age of 24 months has adverse impact on cognition that is not yet fully expressed at age 5 years. A second possibility, not supported by additional analyses, is that different subsets of children were responsible for the associations at the two ages. A third possibility is that this is a measurement artifact stemming from differences in the functional domains assessed by the WISC-R and the McCarthy Scales of Children's Abilities. The associations between pb24 and K-TEA scores were still evident after we adjusted for IQ, suggesting that lead-sensitive behavioral or neuropsychological factors not reflected in WISC-R IQ scores may contribute to reduced performance on academic tasks.

At 24 months of age, children in this cohort had a mean blood lead level of less than 0.34 $\mu\text{mol}/\text{L}$ (7 $\mu\text{g}/\text{dL}$), 90% had levels below 0.63 $\mu\text{mol}/\text{L}$ (13 $\mu\text{g}/\text{dL}$), and all had levels below 1.21 $\mu\text{mol}/\text{L}$ (25 $\mu\text{g}/\text{dL}$). The exposure-related performance differences are approximately twice the size of that observed at 57 months, corresponding to declines of 5.8 and 8.9 points in Full-Scale IQ and K-TEA Battery Composite scores, respectively, for each 0.48- $\mu\text{mol}/\text{L}$ (10- $\mu\text{g}/\text{dL}$) increase in pb24. To provide a context for evaluating the relative importance of lead as a predictor of IQ, children whose mothers achieved IQ scores in the top quartile (in this cohort) had IQ scores that averaged 13.4 points higher than those of children whose mothers' IQ scores were in the bottom quartile. IQ scores of firstborn children averaged 9.0 points higher than those of children born third or later.

Children's performance was much more strongly associated with pb24 than with blood lead levels at other ages. It is unclear whether this reflects a special vulnerability of the nervous system during this period²⁷ or simply the fact that blood lead level tends to peak in the second year.^{4,6-8} Our finding that pb24 was more predictive of performance than was maxi-

TABLE 3. Regression Coefficients Associated With Blood Lead Levels and Children's Kaufman Test of Educational Achievement-Brief Form Scores at 10 Years of Age

Blood Lead Measurement*	Crude: Battery Composite	Adjusted†			
		Battery Composite	Mathematics Composite	Reading Composite	Spelling
10 y	-1.43 (0.63)‡ .025§	-0.44 (0.61) .47	-0.46 (0.71) .52	-0.71 (0.54) .19	-0.24 (0.73) .74
57 mo	-0.80 (0.37) .033	-0.16 (0.34) .64	0.00 (0.41) .99	-0.15 (0.31) .62	-0.35 (0.41) .40
24 mo	-1.09 (0.27) .0001	-0.89 (0.24) .0003	-0.91 (0.29) .002	-0.38 (0.21) .078	-0.97 (0.28) .0008
18 mo	-0.47 (0.24) .050	-0.28 (0.21) .19	-0.31 (0.25) .22	0.08 (0.19) .65	-0.44 (0.25) .077
12 mo	-0.50 (0.21) .018	-0.34 (0.19) .076	-0.40 (0.23) .083	0.08 (.17) .65	-0.41 (0.22) .067
6 mo	-0.14 (0.21) .50	-0.00 (0.18) .99	-0.11 (0.22) .61	0.02 (0.16) .89	0.09 (0.21) .67
Cord					
Low‖	-0.43 (3.32)	0.76 (3.06)	-0.88 (3.62)	-0.35 (2.69)	1.72 (3.58)
Med¶	0.65 (3.36) .95#	-1.55 (2.99) .74	-2.16 (3.55) .83	-3.34 (2.64) .38	-0.44 (3.51) .81

* Age at which blood lead level was measured.

† Adjustment made for the same variables listed in footnote † of Table 2.

‡ Regression coefficient (SE), representing the estimated change in score associated with each 0.48- μ mol/L (1- μ g/dL) increase in blood lead level.

§ Two-sided *P* value associated with the hypothesis that the coefficient is zero.

‖ Coefficient (SE) associated with membership in the "low" cord blood lead group; reference group is children in the "high" cord blood lead group.

¶ Coefficient (SE) associated with membership in the "medium" cord blood lead group; reference group is children in the "high" cord blood lead group.

Two-sided *P* value associated with the hypothesis that there are no differences among the scores of children in the three cord blood lead groups.

mum blood lead level supports the hypothesis of an age-specific vulnerability.

Alternatively, the apparent importance of pb24 as a predictor may be due to methodological factors such as differences in the power of hypothesis tests involving blood lead levels measured at different ages. The extremely low levels, restricted range, and smaller number of 10-year blood lead values reduced the likelihood of finding an association between current exposure and performance. Analyses involving all other postnatal blood lead levels had about 80% power to detect roughly the same effect size ($f^2 = .065$ to $.073$ in Cohen's²⁸ terminology). Other considerations are relevant to this issue, however. The coefficient of variation was substantially greater for pb24 than pb57 (75.0 vs 60.4), suggesting that a greater proportion of the observed variation in pb24 than pb57 reflects differences in children's exposures rather than analytical variation, which was relatively constant over time. Moreover, unlike blood lead levels at 57 months and 10 years, pb24 was not strongly associated with sociodemographic characteristics and psychosocial environment.²⁹ Nevertheless, our finding that, after adjustment for confounding, only blood lead level measured at 24 months was significantly associated with children's function should be interpreted cautiously until confirmed by other studies.

The association was robust to changes in analytical strategy and model composition. Although we cannot exclude the possibility that confounding by some unmeasured or inadequately measured variables produced a spurious association, the estimated decline in

children's scores with increasing pb24 was relatively unaffected by adjustment for a variety of factors germane to the psychological, emotional, and intellectual climate within a family. Nevertheless, measures of such factors are fallible. To the extent that these factors are true confounders and the instruments failed to measure them accurately, our adjustment for confounding bias is incomplete.

Another factor to be weighed in evaluating these results is the possibility of bias in terms of the children available for follow-up. The key issue is whether the associations we observed between lead exposure and development among participants are similar to those we would have observed had we been able to evaluate the entire cohort. We determined that the estimated associations noted at earlier assessments between cord blood lead level and Mental Development Index Scores at 6, 12, 18, and 24 months of age were comparable among children who participated in the 10-year follow-up and those who did not. The degree of similarity in the relationship between pb24 and GCI scores at 57 months is more uncertain because of the relatively small number of children lost to follow-up between 57 months and 10 years. Although the coefficients for participants and nonparticipants were not significantly different, the association between pb24 and performance at 10 years may have been somewhat diminished had we achieved 100% follow-up.

Analyses of WISC-R subtest scores indicated that pb24 was most strongly related to children's scores on verbally mediated tasks. In contrast, at age 57

months pb24 was more strongly associated with non-verbal skills. Verbal deficits among children with higher pb24 levels may not have been apparent at 57 months because of the relative insensitivity of the language assessments available for evaluating children at that age, greater compensatory effects of environmental stimulation on language performance at younger ages, or both. Alternatively, a common underlying neurological substrate (eg, attention, state) that affects performance on psychometric tests may be expressed differently over time. This hypothesis is speculative, although, other follow-up studies have reported that the behavioral and developmental correlates of early biological insult may change over time.³⁰

There is little evidence that lead exposure has a distinctive "behavioral signature." Measures of lead exposure have been significantly related to both Verbal and Performance IQ,³¹ only Verbal IQ,³²⁻³⁶ only Performance IQ,^{37,38} or neither.³⁹⁻⁴³ Findings are also inconsistent with respect to lead and academic achievement.^{33,34,39,41-44} The explanation for this is not clear, although differences in study power may be contributory.⁴⁵ In addition, the manner in which toxicity is expressed may depend on a number of factors, including the timing and level of exposure, its chronicity, and other aspects of a child's developmental context.⁴⁶ Retrospective and cross-sectional studies provide only limited opportunities to discern associations between specific characteristics of exposure history and neuropsychological outcome.

At present, other prospective studies provide only partial support for our findings.^{4-8,47} It is unclear whether this reflects instability of the association between lead exposure and development, methodological differences among studies, or both. The cohorts being followed differ substantially in terms of exposure characteristics. On the basis of toxicokinetic principles, different patterns of associations between exposure and function should be expected.⁴⁸ Functional deficits have consistently been noted at lower blood lead levels in our cohort than in the others. We attribute this, at least in part, to the low background risk of intellectual handicap in this cohort relative to others.⁴⁹ Most US lead studies focus on poor inner-city children for whom lead exposure is only one of many developmental risk factors. The high socioeconomic standing of our cohort may have provided us greater opportunity to perceive lead-related variance in cognitive function. It may also restrict the population to which our findings may be generalized. Early insults tend to be expressed more severely among populations at high socioeconomic risk.⁵⁰ The associations we observed may underestimate those that, with adequate control of confounding, would be observed in a group more representative of children with higher levels of lead exposure.

In summary, this follow-up study of socioeconomically advantaged children with relatively low lifetime exposures to lead suggests that slight elevations of blood lead at around the age of 2 years are associated, without an apparent threshold, with significant decrements in intellectual and academic performance at 10 years of age.

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FAT FACTS

McDonald's merits praise for introducing a lower-fat version of its large hamburger. But by promoting its new "McLean Deluxe" as "91% fat free," it reinforces the trend of using misleading fat-free claims.

Such claims, expressing fat content as a percentage of weight, are a powerful selling tool in a health-conscious market. But much of the weight may be water, so the implication that a product is low in fat can be deceptive. The McLean's 9 percent fat content, for example, though only about half that of standard burgers, still packs 10 grams of fat—five times the FDA definition of low fat.

McDonald's is hardly the only offender. Misleading percentage claims are a marketing ploy for fat-laden products ranging from frozen sausages and french fries to ice cream. The FDA could help consumers by immediately calling for a moratorium on such claims, even while the agency prepares new restrictions to carry out last year's Federal nutrition labeling reform.

Fat facts. *The New York Times*. April 23, 1991.

Submitted by Kurt Metzl, MD